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Carmi

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(54) **PERFUSION IMAGING**

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(Continued)

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G06T 15/08; G06T 2200/04; G06T 2207/10076; G06T 2207/10081; G06T 2207/30024; G06T 2207/30061; G06T 2207/30101; G06T 2210/41; G06T 2211/40; A61B 6/032; A61B 6/504
See application file for complete search history.

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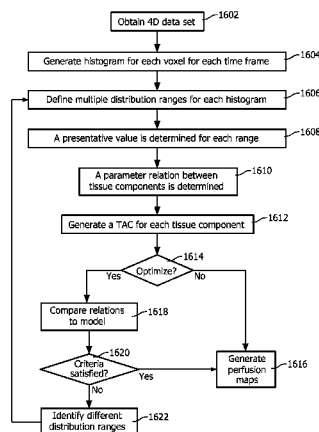(Continued)

Primary Examiner — Katrina Fujita

(57) **ABSTRACT**

Described herein is an approach for analyzing perfusion characteristics of heterogeneous tissues in 4D data set (i.e., a time series of contrast enhanced 3D volumes) in which spatially entangled tissue components are separated into individual tissue components and perfusion maps for the individual tissue components are generated and visually presented. In one instance, the approach includes obtaining the 4D data set in electronic format, generating a different time activity curve point for each of the different tissue components for each voxel being evaluated for each time frame being evaluated, and generating a signal indicative of a different parameter map for each of the different tissue components based at least on the time activity curves. Optionally, relations between parameters of the different components are determined and presented in relation maps.

20 Claims, 12 Drawing Sheets

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    A61B 6/00   (2006.01)
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(52) **U.S. Cl.**
    CPC *G06T 7/0081* (2013.01); *G06T 15/08*
        (2013.01); *G06T 2200/04* (2013.01); *G06T*
        2207/10076 (2013.01); *G06T 2207/10081*
        (2013.01); *G06T 2207/30024* (2013.01); *G06T*
        2207/30061 (2013.01); *G06T 2207/30101*
        (2013.01); *G06T 2210/41* (2013.01); *G06T*
        2211/40 (2013.01)

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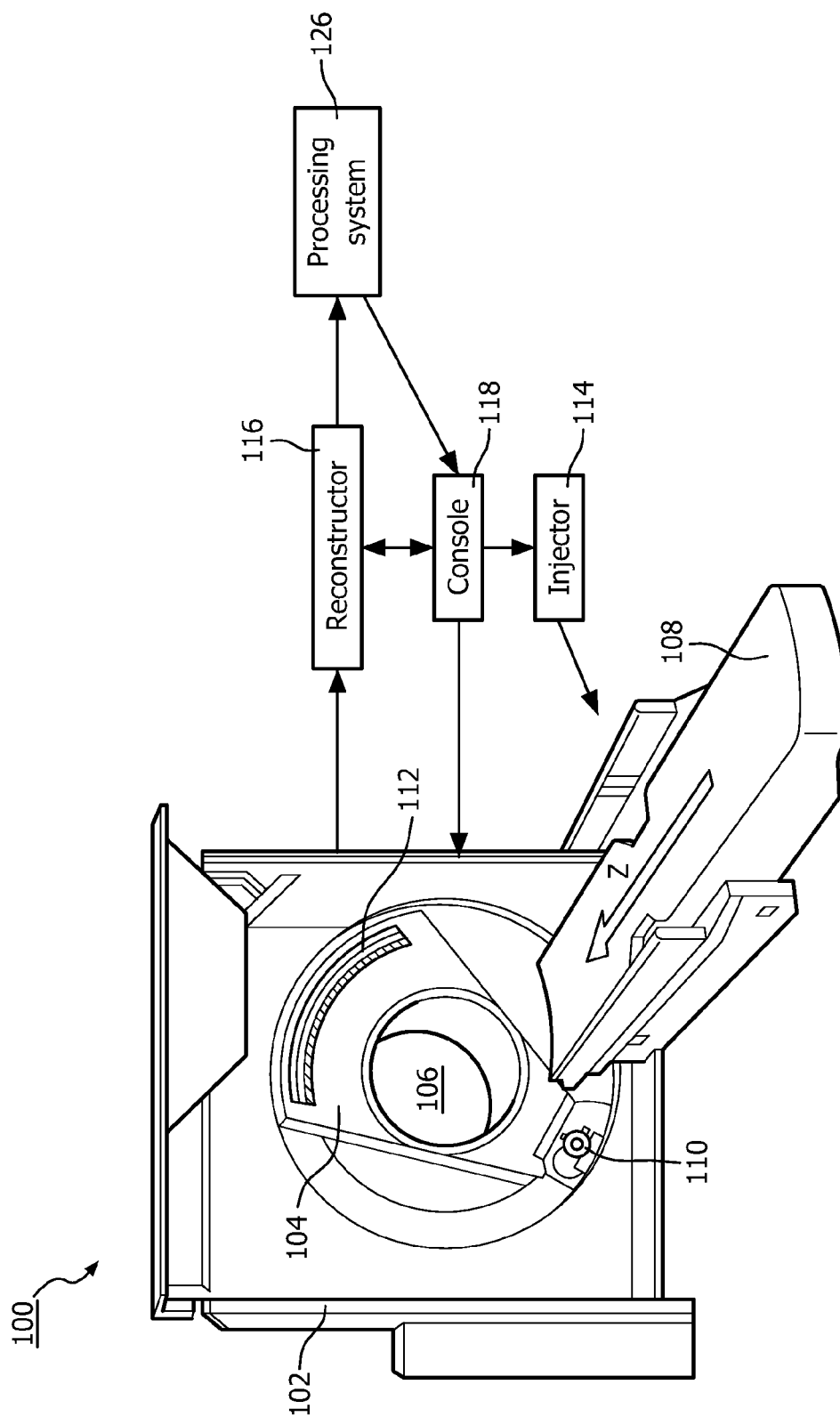
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FIG. 1

Processing system

200 — Mask generator

202 — Mask applier

204 — Histogram generator

208 — Tissue class memory

216 — Tac generator

222 — Rendering engine

206 — Histogram evaluator

210 — Histogram divider

212 — Histogram representative value determiner

214 — Parameter determiner

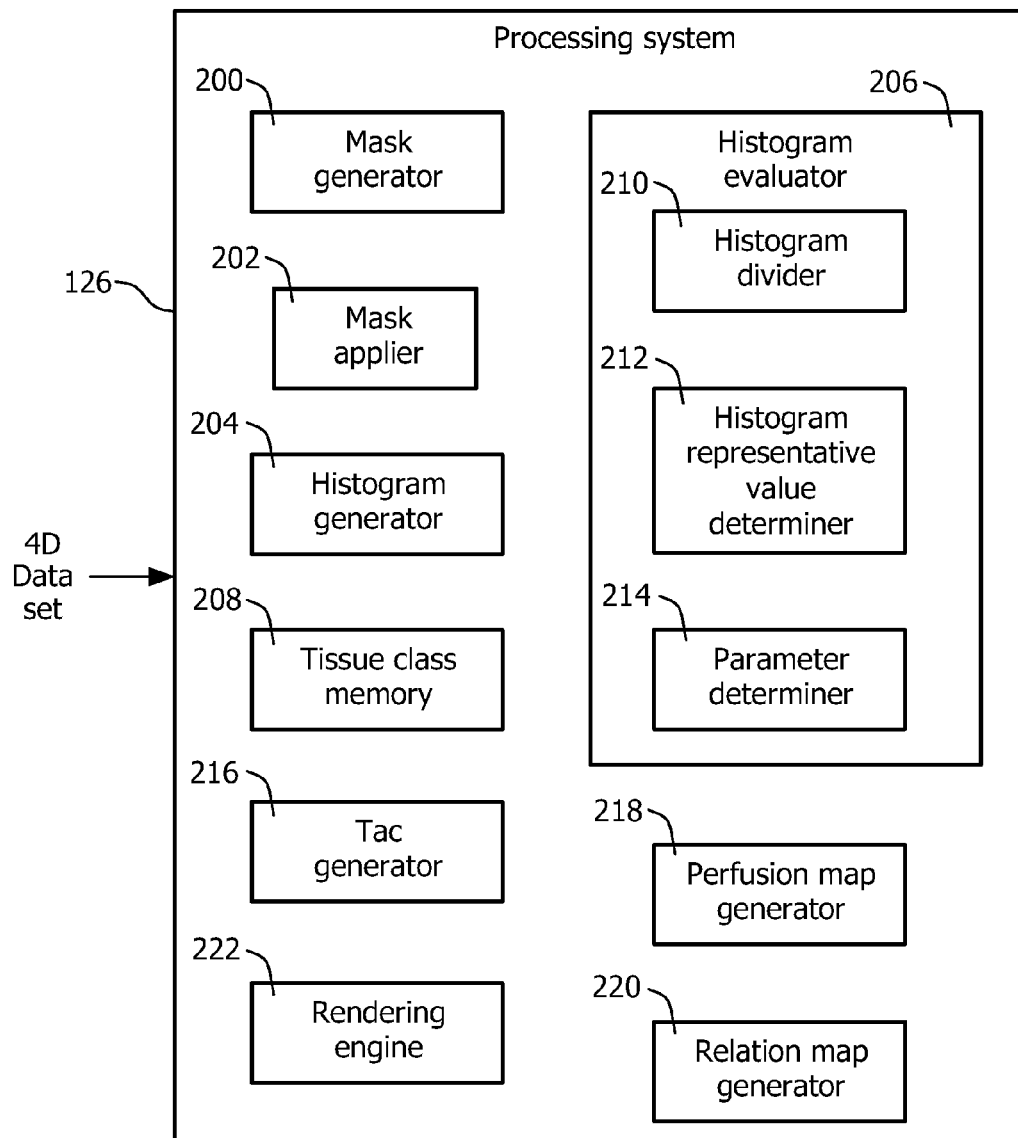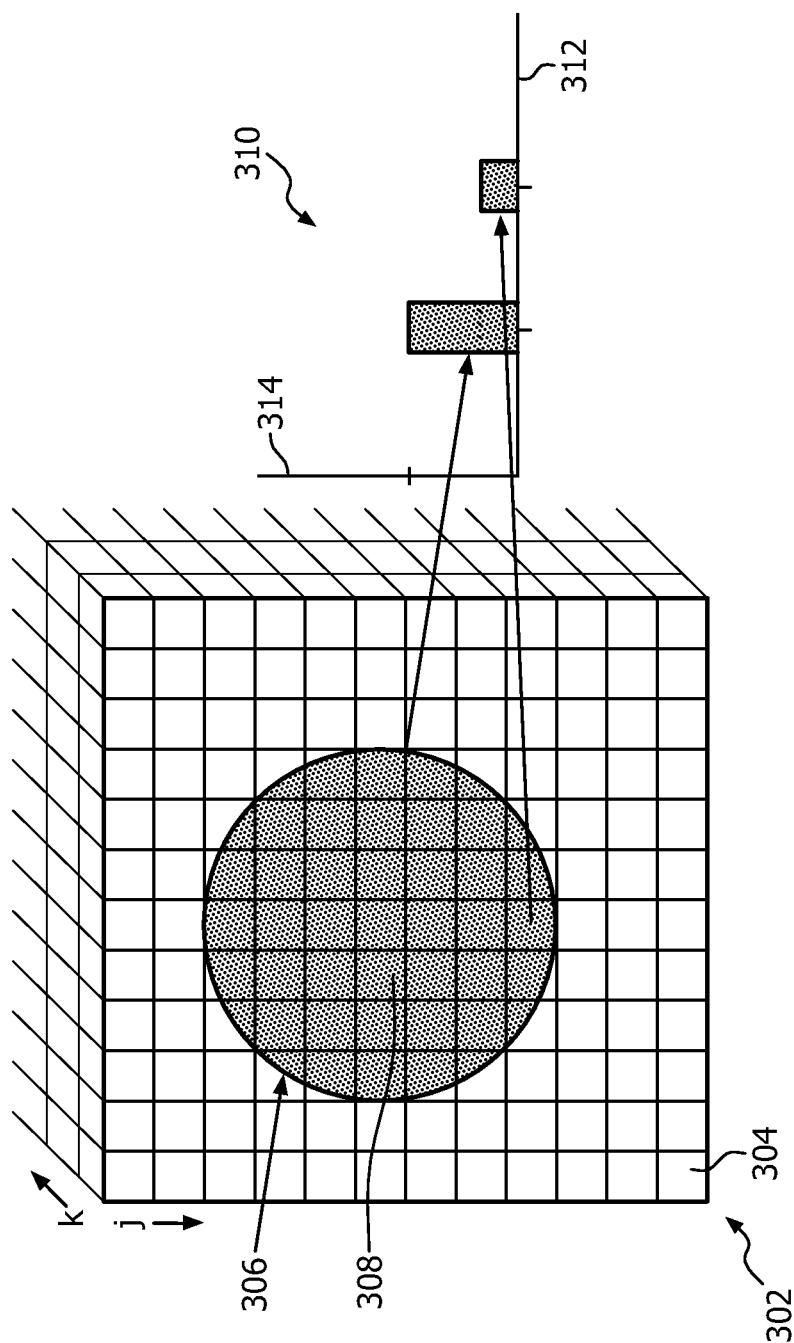218 — Perfusion map generator
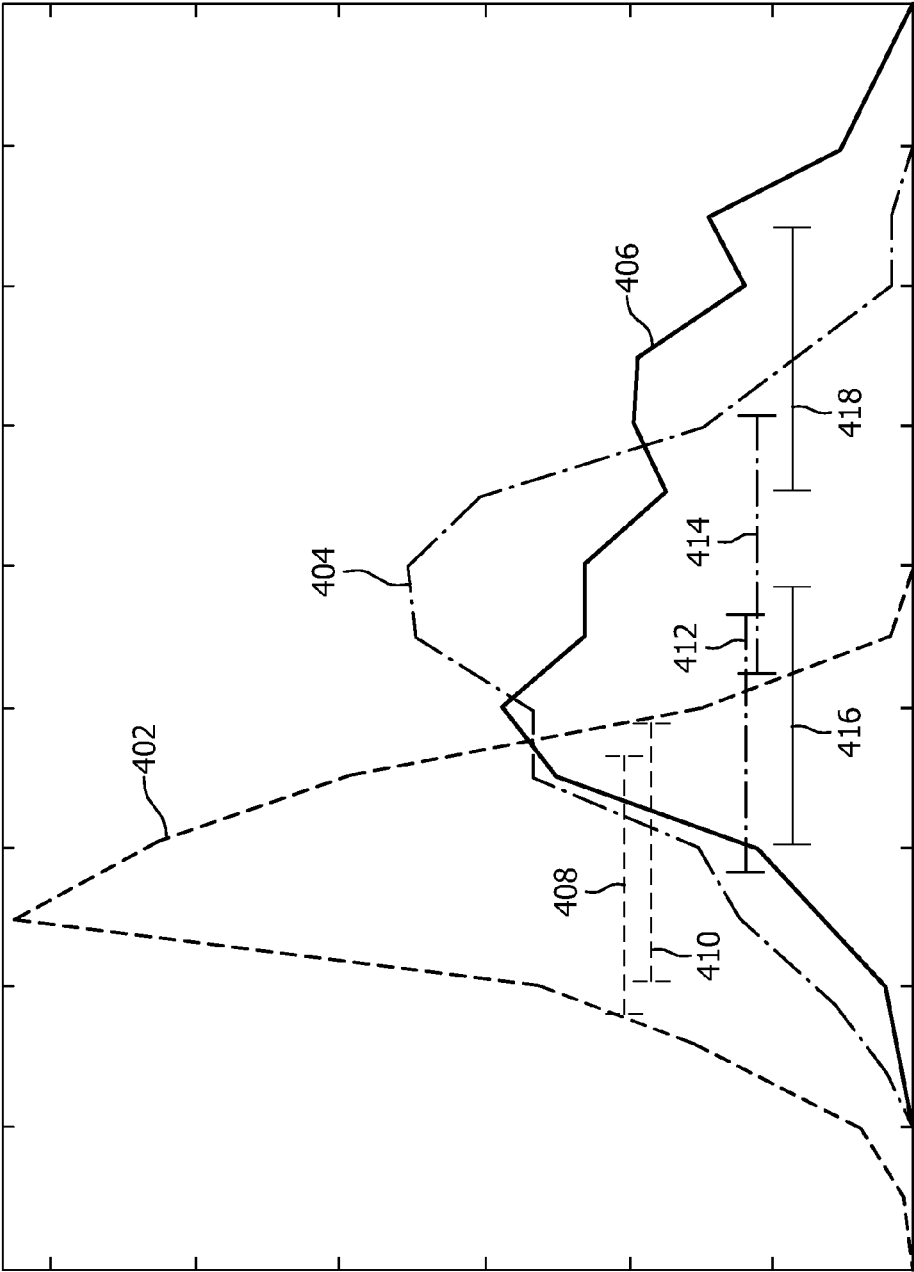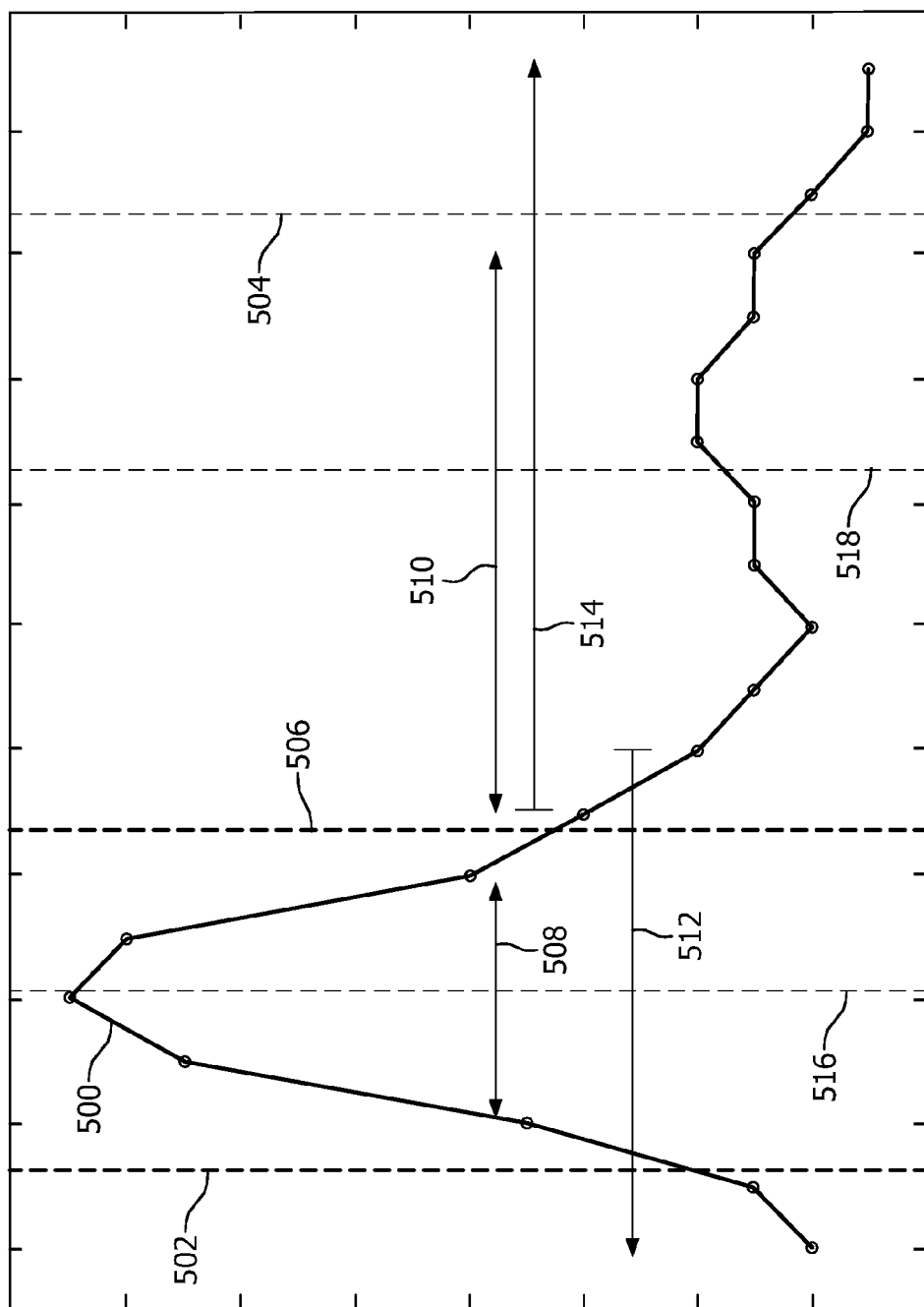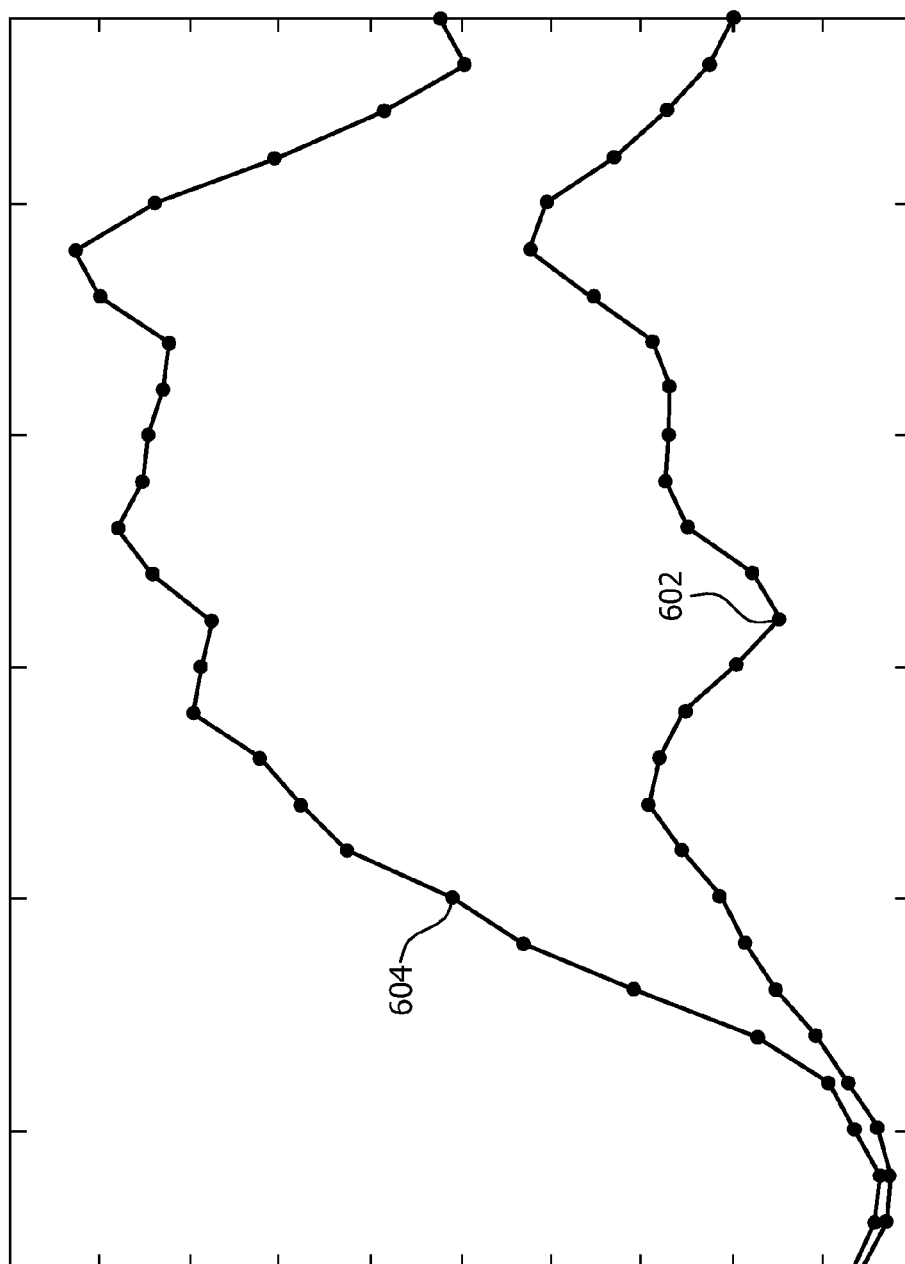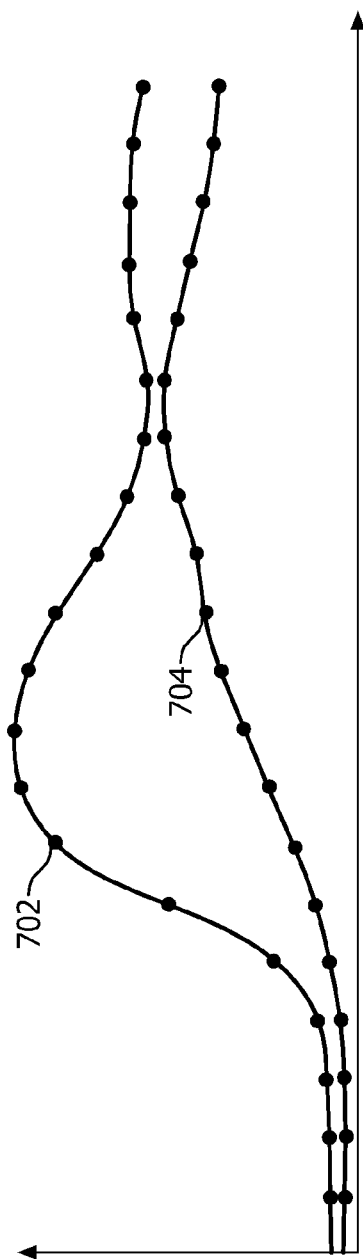
220 — Relation map generator

126 —

4D Data set →

FIG. 2

FIG. 3

FIG. 4

FIG. 5

FIG. 6

FIG. 7
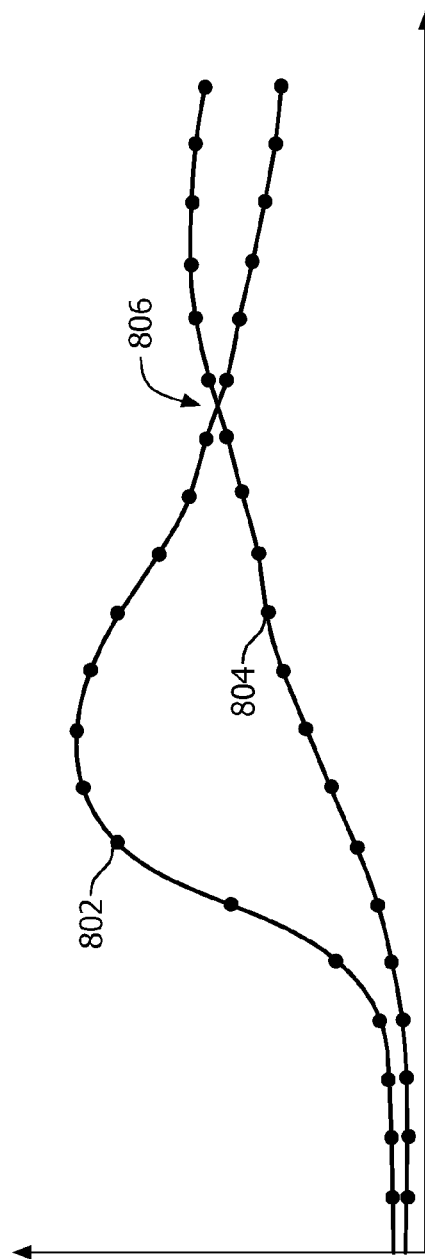
FIG. 8
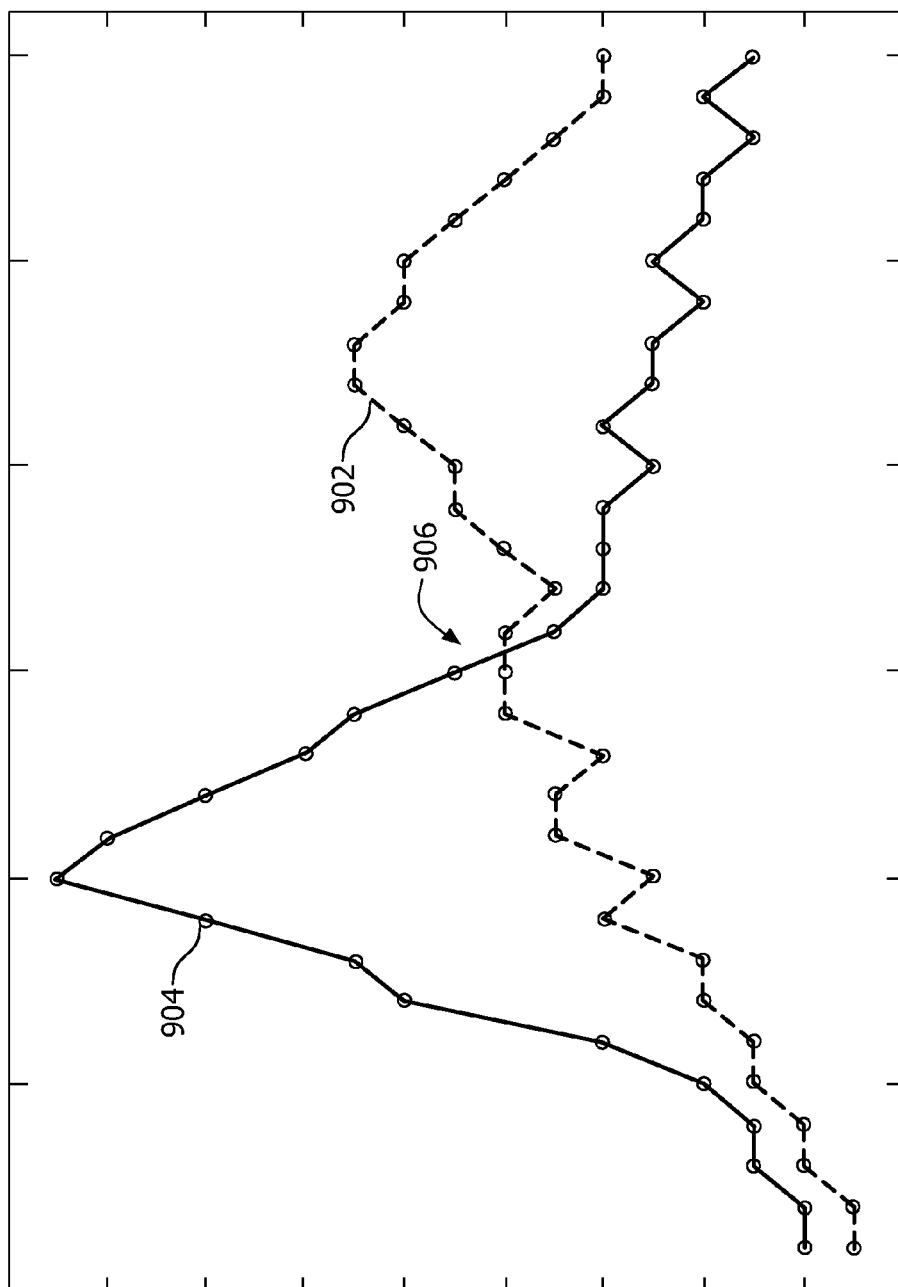
FIG. 9
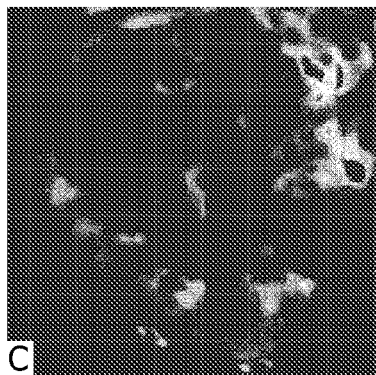
FIG. 10
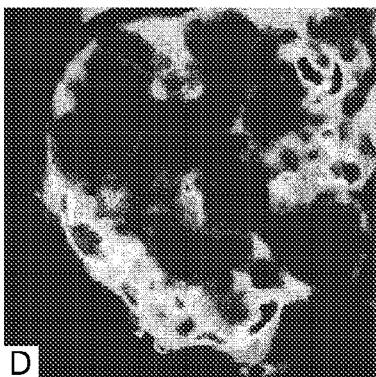
FIG. 11
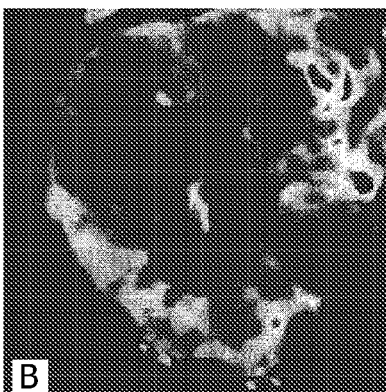
FIG. 12
(Prior Art)

FIG. 13

FIG. 14

Processing system

202 — Mask generator

202 — Mask applier

126

204 — Histogram generator

208 — Tissue class memory

4D data set → 216 — Tac generator

222 — Rendering engine

Histogram evaluator

210 — Histogram divider

212 — Histogram representative value determiner

214 — Parameter determiner

206

218 — Perfusion map generator

220 — Relation map generator

1502

Optimizer

1504 — Analyzer   1506 — Mode

1508 — Criteria checker   1510 — Criteria

FIG. 15

Obtain 4D data set ⟵1602

Generate histogram for each voxel for each time frame ⟵1604

Define multiple distribution ranges for each histogram ⟵1606

A presentative value is determined for each range ⟵1608

A parameter relation between tissue components is determined ⟵1610

Generate a TAC for each tissue component ⟵1612

Optimize? ⟵1614

Yes   No

Compare relations to model ⟵1618

Criteria satisfied? ⟵1620

Yes

Generate perfusion maps ⟵1616

No

Identify different distribution ranges ⟵1622

FIG. 16

PERFUSION IMAGING

CROSS REFERENCE TO RELATED APPLICATIONS

This application is a national filing of PCT application Serial No. PCT/IB2013/059829, filed Oct. 31, 2013, published as WO 2014/068520 A1 on May 8, 2014, which claims the benefit of U.S. provisional application Ser. No. 61/720,475 filed Oct. 31, 2012, which is incorporated herein by reference.
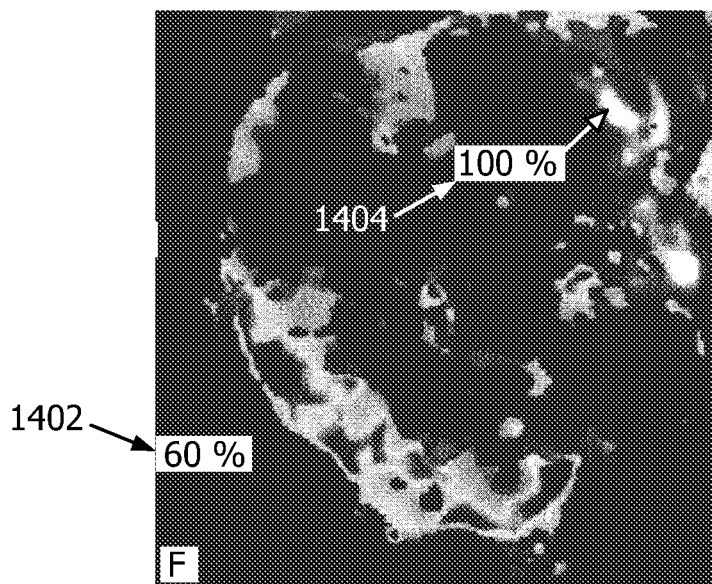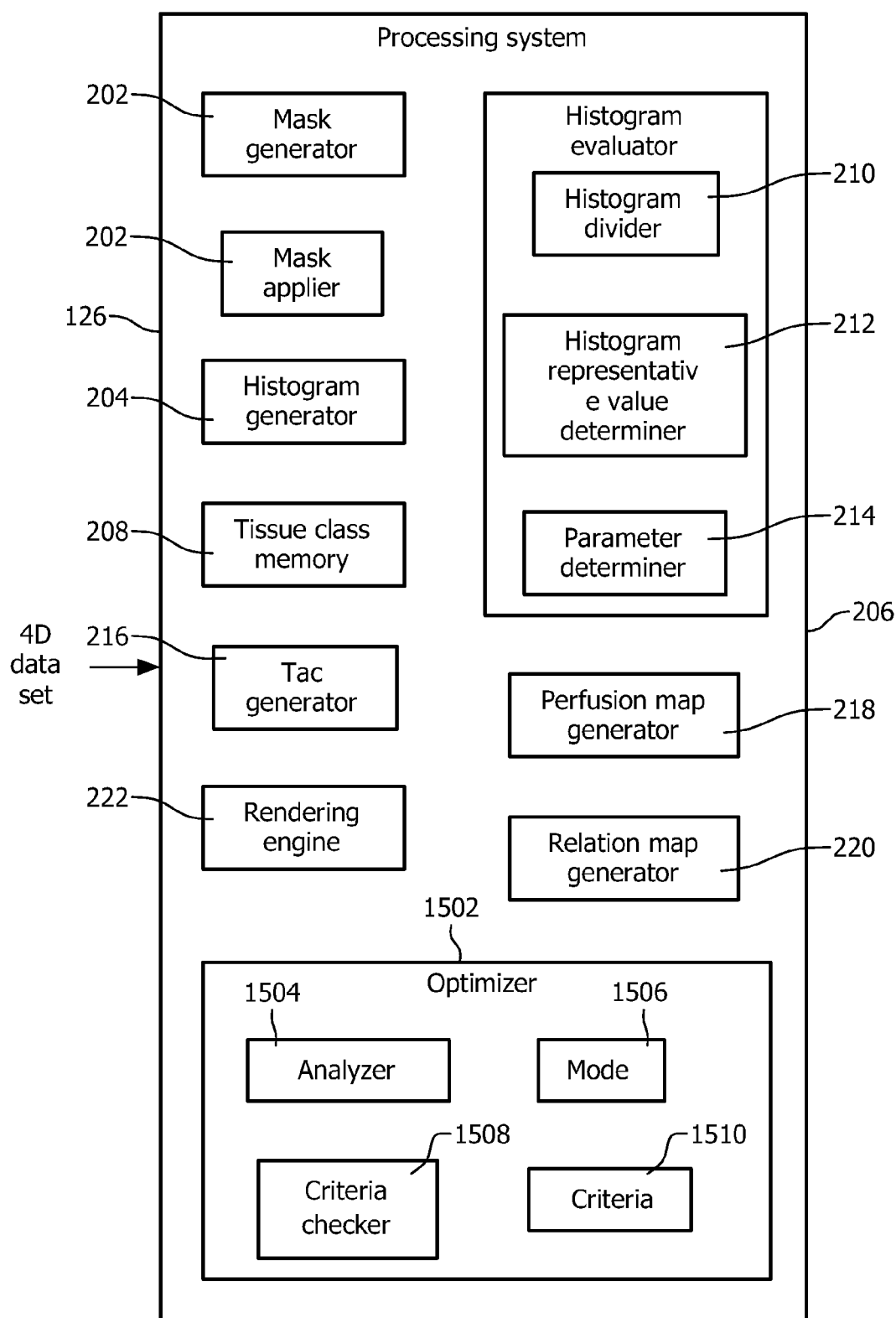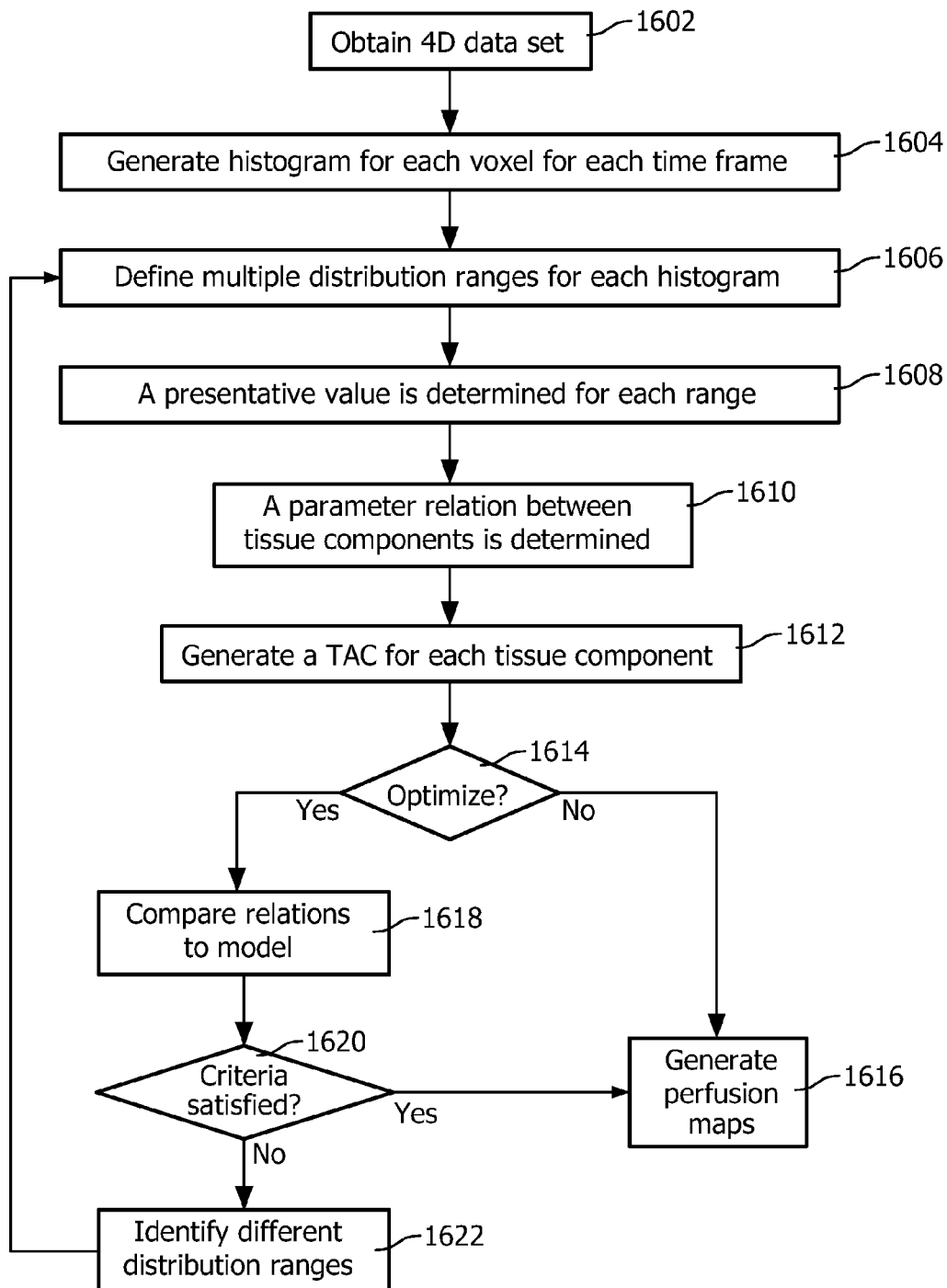
The following generally relates to perfusion imaging and is described with particular application to computed tomography (CT); however, the following is also amenable to other imaging modalities including magnetic resonance imaging (MRI), positron emission tomography (PET), single photon emission computed tomography (SPECT), ultrasound (US) and/or other imaging modalities.

CT perfusion imaging provides functional information through imaging characteristics related to the blood flow in organs and tissues using a contrast material such as iodine contrast agent. A typical perfusion study requires repeated imaging of the volume of interest for a number of different time points, for example, 3-30 repeated scans with a few seconds difference between successive scans (e.g. 1 to 10 sec per time frame). In common perfusion techniques, a bolus of a contrast agent is administered into the patient's vascular system and images from the region of interest are collected for a period covering the transit of the contrast agent bolus through the tissue in the region of interest.

The local concentration changes of the contrast agent over time are used for analyzing physiological parameters. In clinical practice, it is common for the perfusion image series to be inspected qualitatively or to be assessed quantitatively with special analysis algorithms. A quantified result may include, for a region or per voxel, a measurement of blood flow, blood volume, mean transit time, time of arrival, permeability, time to peak, peak intensity, maximal gradient, and/or other parameters. Perfusion imaging of heterogeneous tissues, which is relevant to many tumor types and/or other tissue, often poses challenges for accurate perfusion quantification.

By way of example, different tissue components can be spatially entangled within a region of interest and, thus, even subtle patient or organ motion during the dynamic acquisition can introduce significant analysis errors as the time series may not be spatially-aligned. One approach to reduce this has been to smooth the images and to calculate average perfusion values of the organ regions. Another approach to reduce this has been to analyze, collectively, the voxels in a region of interest, e.g., by using histogram or segmentation techniques. Unfortunately, such approaches still do not provide comprehensive analysis of perfusion parameters of heterogeneous tissues.

Aspects described herein address the above-referenced problems and others.

The following describes an approach for analyzing perfusion characteristics of spatially entangled heterogeneous tissues in 4D image data (i.e., a time series of contrast enhanced 3D volumes) in which spatially entangled tissue components are separated and perfusion maps for the individual tissue components are generated and visually presented.

In one aspect, a method includes obtaining a 4D data set in electronic format, wherein the 4D data set includes a plurality of 3D volumes of voxels of contrast enhanced perfusion imaging data for two or more time frames, and the

3D volumes include data representative of at least two different tissue components in a same region of interest in at least one of the time frames, generating a different time activity curve point for each of the different tissue components for each voxel being evaluated for each time frame being evaluated, and generating a signal indicative of a different parameter map for each of the different tissue components based at least on the time activity curves.

In another aspect, a processing system includes a histogram generator that generates a histogram for each voxel being evaluated in a plurality of 3D volumes of voxels of contrast enhanced perfusion imaging data for two or more time frames, wherein the 3D volumes include data representative of at least two different tissue components in a same region of interest in at least one of the time frames, a time activity curve (TAC) generator that generates a different time activity curve point for each of the different tissue components for each voxel being evaluated for each time frame being evaluated, and perfusion map generator that generates a signal indicative of a different parameter map for each of the different tissue components based at least on the time activity curves.

In another aspect, an imaging system includes a computer readable storage medium encoded with one or more computer executable instructions, which, when executed by a processor of a computing system, causes the processor to: analyze perfusion characteristics of heterogeneous tissue by separating spatially entangled tissue components into two or more tissue classes and generating a set of perfusion maps for each of the individual tissue components.

The invention may take form in various components and arrangements of components, and in various steps and arrangements of steps. The drawings are only for purposes of illustrating the preferred embodiments and are not to be construed as limiting the invention.

FIG. **1** schematically illustrates an example processing system in connection with an imaging system.

FIG. **2** schematically illustrates an example of the processing system of FIG. **1**.

FIG. **3** illustrates a portion of volumetric image, a weighted mask, and a weighted histogram.

FIG. **4** illustrates example weighted histograms for a voxel for different volumes of the time series and tissue component ranges therein.

FIG. **5** illustrates an example of a weighted histogram for a voxel for a volume of the time series and tissue component ranges therein.

FIG. **6** illustrates example multiple TACs generated for different tissue components from a histogram.

FIG. **7** illustrates a first model for determining the multiple TACs of FIG. **6**.

FIG. **8** illustrates a second different model for determining the multiple TACs of FIG. **6**.

FIG. **9** illustrates another example of multiple TACs generated for different tissue components from a histogram.

FIG. **10** illustrates a perfusion map for one of a plurality of separated entangled tissue components.

FIG. **11** illustrates a perfusion map for a second of the plurality of separated entangled tissue components.

FIG. **12** illustrates a prior art perfusion map, where the tissue components are not separated, after smoothing the image data of all time frames

FIG. **13** illustrates a relation map for one of a plurality of separated entangled tissue components.

FIG. **14** illustrates a relation map for another of the plurality of separated entangled tissue components.

FIG. **15** schematically illustrates a variation of the processing system which includes an optimizer.

FIG. **16** schematically illustrates a method for separating spatially entangled heterogeneous tissue components.

The following describes an approach for analyzing perfusion characteristics of spatially entangled heterogeneous tissues in 4D image data in which spatially entangled tissue components are separated and perfusion maps for the individual tissue components are generated and visually presented.

FIG. **1** schematically illustrates an example imaging system **100** such as a CT scanner. In other embodiments, the imaging system **100** can include one or more of an MRI, PET, SPECT, US, a combination thereof, and/or other imaging system configured to perform dynamic contrast enhanced imaging scans. The illustrated imaging system **100** includes a stationary gantry **102** and a rotating gantry **104**, which is rotatably supported by the stationary gantry **102** and rotates around an examination region **106** about a z-axis.

A radiation source **110**, such as an x-ray tube, is rotatably supported by the rotating gantry **104**, rotates with the rotating gantry **104**, and emits polychromatic radiation that traverses the examination region **106**. A radiation sensitive detector array **112** subtends an angular arc opposite the radiation source **110** across the examination region **106**, detects radiation traversing the examination region **106**, and generates a signal indicative thereof. A subject support **108** supports an object or subject in the examination region **106**.

An optional injector **114** is configured to inject a contrast material(s), for example, for a contrast enhanced imaging procedure, such as a perfusion scan. The illustrated injector **114** is controlled by the imaging system **100**, which may trigger or invoke in the injector **114** to administer the contrast material. A contrast material(s) can alternatively be manually administered by a clinician or the like. Where the contrast material(s) is manually administered, the injector **114** can be omitted.

A reconstructor **116** reconstructs the projection data, generating volumetric image data. For perfusion imaging, this includes reconstructing a time series of contrast enhanced volumetric (3D) image data (or 4D data set) indicative of perfusion through scanned tissue of interest. A general-purpose computer serves as an operator console **118**. Software resident on the console **118** allows the operator to interact with the scanner **100**, e.g., to select a perfusion imaging protocol.

A processing system **126** processes 4D data sets generated by the imaging system **100** and/or other imaging system. In the illustrated embodiment, the processing system **126** obtains the 4D data set from the imaging system **100**. In another instance, the processing system **126** obtains the 4D data set from a storage medium, for example, portable memory, a server, a database, a radiology information system (RIS), hospital information system (HIS), an electronic medical record (EMR), picture archive and communication system (PACS), and/or other data repository.

As described in greater detail below, the processing system **126** is configured to separate spatially entangled heterogeneous tissue components (classes) of scanned tissue into at least two different components, which allows for generating two or more different sets of perfusion maps for the same spatial region (voxel) of tissue, including an individual map for each of the tissue components. Examples of such tissue include, but are not limited to, normal tissue, tumoral tissue, liver tissue, lung tissue, a tissue region which includes a network or a mesh of small blood vessels passing

through an organ parenchyma, and/or a mesh-like structure of lung tissue and air pockets between small segments of the tissue mesh.

The processing system **126** can be implemented via one or more processors executing one or more computer readable instructions embedded, encoded, etc. on computer readable storage medium such as physical memory and/or other non-transitory medium. Additionally or alternatively, at least one of the computer readable instructions can be carried by a carrier wave, signal, and/or other transitory medium.

FIG. **2** schematically illustrates an example of the processing system **126**. As shown, the processing system **126** receives as input the 4D data set.

A mask generator **200** generates a mask of weights to weight values of voxels surrounding a voxel (or region of voxels) of interest currently being analyzed, and a mask applier **202** applies the mask to the voxel being analyzed. FIG. **3** shows a volume **302** of voxels **304** with a 3D Gaussian mask **306** applied thereto. The mask **306** has a defined sigma value (or width) and a defined cut-off in a certain radius distance from a voxel **308**. Portions of voxels adjacent to the voxel **308** are weighted with a value close to one (1), and the value of the weights falls off with a distance of a voxel from the voxel **308**. Other weighting functions (e.g., binary, linear, exponential, stepped, etc.) are also contemplated herein.

With reference to FIGS. **2** and **3**, a histogram generator **204** generates a weighted histogram **310** for one or more of the voxels **304** and one or more time frames, e.g., each or a subset of the voxels **304** and/or the time frames based on the mask **306**. In the example histogram **310**, an x-axis **312** represents a value indicative of the image information (e.g., Hounsfield units in a CT image) and a y-axis **314** represents a value indicative a number of voxels for each HU value, after multiplying a contribution of each voxel **304** by a corresponding weight from the mask **306**. For clarity and sake of brevity, FIG. **3** shows weighted contributions of only two of the voxels **304** and one time frame.

With the mask **306**, if a voxel **304** is relatively far from the voxel **308** of interest, then the contribution of the voxel to the histogram in the y-axis **314** will be proportionally reduced, but its contribution to the x-axis **312** is not changed. In this way, a shape of the histogram **310** corresponding to a certain spatial position will not be very sensitive to any tissue miss-alignment between the successive time frames of the scan caused by motion and/or otherwise. In addition, the weighting pattern, which is decreased gradually out of the central voxel, will contribute to less-patchy perfusion maps. Generally, a histogram represents weighted image information surrounding an analyzed voxel.

By way of a more specific example, a non-limiting suitable 3D Gaussian mask **306** can be defined as $W_0(i,j,k)=\exp(-(i^2 \cdot r_x^2 + j^2 \cdot r_y^2 + k^2 \cdot r_z^2)/2/\xi^2)$, where $[r_x, r_y, r_z]$ are the directional mm/pixel scaling in the image volume, $[i,j,k]$ are the indexes (around the voxel of interest $[0,0,0]$) for which W_0 is above a determined threshold. A normalized weight mask W can be derived to satisfy $\Sigma W=1$. The Gaussian width ξ (in mm) determines the histogram 'clustering length'. The histogram bin partition in the relevant Hounsfield unit (HU) range is pre-defined. The weighted histogram is constructed in a process in which each voxel which is covered by the mask (in the vicinity of the voxel of interest) adds the corresponding mask weight to the height of the histogram bin which comprises the image voxel HU value. In this way, the weighting pattern, which is decreased gradually out of the central voxel, will contribute to smooth and less-patchy perfusion maps.

With respect to FIG. 2, a histogram evaluator 206 evaluates the weighted histograms and determines a representative value for each tissue component. In this example, the number of tissue components is pre-defined and stored in tissue class memory 208. In another instance, the number of tissue components is identified via a signal indicative of an user input identifying a desired number of tissue components, automatically determined based on 4D data set (e.g., based on the tissue scanned, the imaging protocol), etc. For sake of brevity and clarity, the following will describe an example in which the number of tissue components is two (2).

FIG. 4 shows three example histograms 402, 404, and 406 respectively representative of a same voxel for three different time frames. With reference to FIGS. 2 and 4, the histogram evaluator 206 includes a histogram divider 210 that divides each histogram into a number of sections or ranges equal to the number of components. As shown, the histogram 402 is divided into sections 408 and 410, which have equal widths and higher overlap (>50% overlap), the histogram 404 is divided into sections 412 and 414, which have equal widths and lower overlap (<50% overlap), and the histogram 406 is divided into sections 416 and 418, which have equal widths and no overlap, including a gap.

In another instance, at least two of the ranges have different widths. The histogram evaluator 206 further includes a histogram representative value determiner 212 that determines a representative value for each of the sections 408-418. In this example, the histogram representative value determiner 212 determines a representative value by determining a momentum (e.g., first, second, or higher order) around each section of the sections 408-418. The widths can further define weights for calculating the momentum. Other approaches are also contemplated herein.

FIG. 5 illustrates another example. For this example, a single histogram 500 analysis for two tissue components is described.

With reference to FIGS. 2 and 5, the histogram divider 210 determines a lower threshold 502 as a HU value above histogram data points from a lower HU range, which, in the illustrated embodiment, represents an area below 5% (or other percent) of the total area, and a higher threshold 504 as a HU value below the histogram data points from a higher HU range, which, in the illustrated embodiment, has the area below 5% (or other percent) of the total area. The histogram representative value determiner 212 calculates a "center of gravity" 506 of the total histogram 500, for example, as (Σ $x_i \cdot y_i$)/(Σ y_i), where y_i are the histogram bin heights and x_i are the HU values of the bin positions. The histogram representative value determiner 212 calculates a HU range 508 of the histogram 500 between 502 and 506, and calculates a HU range 510 of the histogram 500 between 506 and 504.

If a length of 508 is less than a predetermined model parameter, then 508 is extended to a right side by a difference between the model parameter and the length (or until the right margin of the histogram, if it is narrower). In the illustrated example, the length of 508 is less than the model parameter and thus extended to the right. The length 508 is also extended to the lower HU margin of the histogram, creating the range 512. If a length of 510 is less than the model parameter, then 510 is extended to a left side by a difference between the model parameter and the length (or until the left margin of the histogram, if it is narrower). In the illustrated example, this is not required since the length of 510 is greater than the model parameter. The length 510 is also extended to the higher HU margin 504 of the histogram 500, creating the range 514.

The histogram representative value determiner 212 calculates a "center of gravity" 516 for the range 512. For this, the data points which are covered both by 512 and 514 (two points in the example) contribute half of their values to the "center of gravity" calculation of the 512 range, determining 516. The histogram representative value determiner 212 calculates a "center of gravity" 518 for the range 514. For this, the data points which are covered both by 512 and 514 (two points in the example) contribute half of their values to the "center of gravity" calculation of the 514 range, determining 518. The HU values 516 and 518 are the representative distribution values of the two tissue components in this position and time frame.

With respect of FIG. 2, a parameter determiner 214 determines one or more parameters from the histograms. For example, in one instance, the optional parameter determiner 214 determines relations between the relative-volumes of the different components based on the histograms. The relative-volume of a tissue class can be determined as the weighted area in a relevant section of a histogram. The parameter relation can be determined as a ratio, for example, between the relative-volume of the tissue components (or other similar function). Other parameter relations are also contemplated herein.

By way of further example, in connection with FIGS. 2 and 5, the parameter determiner 214 calculates a total area under the histogram values of range 512 divided by the total histogram area and calculates a total area under the histogram values of range 514 divided by the total histogram area. For both cases, the data points which are covered both by 512 and 514 (two points in the example) contribute half of their values to the sum of the values in 512 and 514. In the illustrated example, the result for the first relative volume is 66.3% and the result for the second relative volume is 33.7%.

With respect of FIG. 2, a time activity curve (TAC) generator 216 generates time activity curves (TACs) for the voxels 304 based on the sections of the histograms. Continuing with the above example with two tissue classes, two TAC points are generated for each histogram, one TAC point for each section. FIG. 6 shows an example of two TACs 602 and 604 for sets of two sections of each histogram along the measured time frames. To determine the two TACs 602 and 604, the TAC generator 216 employs an algorithm that finds which of the data points (of a specific time frame) belongs to each of the tissue classes. For this, a model of the blood flow pattern in the relevant presumed tissue can be used to facilitate determining this information.

FIGS. 7 and 8 show examples of such a model. In FIG. 7, the model assumes (e.g., based on an a priori knowledge about the organ) that a single circulatory flow is relevant (e.g. an arterial flow only). As such, an example division pattern is one tissue class (profile 702) that mainly contains blood vessels and has a higher contrast enhancement and a second tissue class (profile 704) such as an organ parenchyma that has a lower contrast enhancement. In FIG. 8, two different circulatory flows are assumed, a first flow in a first tissue class (profile 802) and a second flow in a second tissue class (profile 804). In this example, the two profiles 802 and 804 cross at 806.

With reference to FIGS. 5 and 9, another example in which points in a pair of TAC values belong to each of the two tissue classes. Following FIG. 5, there are two data points for each time frame. The TAC generator 216 first determines which of the two data points in each time frame belongs to the first tissue component and which to the second tissue component. Generally, the type of perfusion

patterns in the scanned organ can be predicted. For example, in the lung tissues there can be the earlier pulmonary circulation and the later arterial circulation, in the liver there can be the earlier arterial circulation and the later hepatic portal circulation, in many other organs, only arterial circulation is possible, etc.

In a simple case, where only a single circulation is predicted, the model can select in each time frame a lowest data point in a pair for a first tissue component, and a highest data point in a pair for the second tissue component, as shown in FIG. **6**. This will result in the first TAC **602** with relatively low perfusion and the second TAC **604** with relatively high perfusion. In a more complicated case, where two different circulations are predicted, other model conditions can be determined. An example for such a model is related to the data points in FIG. **9**. With this model, data points are grouped in such a way that a sum of the two absolute values of the two second derivatives is minimal. In a discrete form, the second derivative (for an arbitrary vector z) is: $z(i)+z(i-2)-2*z(i-1)$.

More particularly, in a data set with N time frames and two initial data sets $y1(1:N)$ of the lower values (of each pair) and $y2(1:N)$ of the higher values (of each pair), the values in two TACs $c1(1:N)$ and $c2(1:N)$ are arranged in such a way that they will fit the defined model (in this example, the minimal second derivatives). In the simple scheme below, the first two time frames are determined in a trivial way, and the other time frames are determined serially according to the conditions:

```
Set: c1(1)=y1(1); c2(1)=y2(1); c1(2)=y1(2); c2(2)=y2(2);
for i=3:N
    g1=abs(y1(i)+c1(i-2)-2*c1(i-1))+abs(y2(i)+c2(i-2)-2*c2(i-1));
    g2=abs(y2(i)+c1(i-2)-2*c1(i-1))+abs(y1(i)+c2(i-2)-2*c2(i-1));
    if g1>g2
        c1(i)=y2(i);
        c2(i)=y1(i);
    else
        c1(i)=y1(i);
        c2(i)=y2(i);
    end
end
```

Two calculated TACs **902** and **904** are shown in FIG. **9** and represent correctly the arterial circulation and the portal circulation in a simulated liver scan data. The correct identification of a crossing region **906** of the two TACs is a result of the model condition. It is also possible to add conditions for robustness against noise such as data smoothing and checking curve derivative on different scales.

Returning to FIG. **2**, a perfusion map generator **218** generates one or more perfusion maps based on the TACs. The volumetric perfusion maps can be calculated using a standard or other technique and include maps for blood flow, blood volume, mean transit time, time of arrival, permeability, time to peak, peak intensity, maximal gradient, and/or other parameters. FIGS. **10** and **11** respectively show a first perfusion map of a first tissue-component with a lower perfusion and a second perfusion map of a second tissue-component with a higher perfusion. FIG. **12** shows a prior art perfusion map, where the tissue components are not separated, after smoothing the image data of all time frames.

Where the parameter determiner **214** determines relations between the relative-volumes of the different tissues classes based on the histograms, a relation map generator **220** generates a parameter relation map between the tissue components. FIGS. **13** and **14** show examples of such a map, in grayscale. Optionally, color can additionally or alterna-

tively be used. For FIGS. **13** and **14**, if the two tissue classes are likely identical (i.e. the voxel contains a single tissue component), then the voxel is represented via a predetermined gray level. A grayscale (or a color scale) is used for voxels including at least two tissue classes.

In the illustrated example, in response to hovering a curser over a voxel in FIG. **13** or **14**, a relative contribution of a tissue component in the image is presented, as shown at **1302**, **1304**, **1402** and **1404** in FIGS. **13** and **14**. By way of example, in the illustrated embodiment, a first tissue component is shown at **1302** to be 40% of the tissue at that voxel and a second tissue component is shown at **1402** to be 60% of the tissue at that voxel. A same single tissue component (e.g., the first component, the second component or another component) is shown at **1304** and **1404** to be 100% of the tissue at that voxel.

A rendering engine **222** visually presents one or more of the perfusion maps (FIGS. **10** and **11**) and/or relation maps (FIGS. **13** and **14**).

FIG. **15** shows a variation of FIG. **2** in which the processing system **126** further includes an optimizer **1502**. The optimizer **1502** includes an analyzer **1504** that compares the time series of the tissue parameter relation values with a pre-defined model **1506**, which defines a likelihood of the parameter relation pattern between the multiple tissue classes. A criteria checker **1508** checks the result of the comparison against pre-determined criteria **1510**.

If the result satisfies the pre-determined criteria **1510**, the generated TACs are utilized to generate the parameter maps as discussed above. If not, the histogram divider **210** is invoked to employ a different set of ranges for each histogram for a subsequent TAC generation iteration. Such iterations can be repeated until the optimization criteria are met, pre-defined limits of iteration numbers is reached, a change between iteration results is sufficiently small, a predetermined processing time elapses, etc.

By way of a more detailed non-limiting example, after determining the TACs, each point in a TAC has its calculated relative volume (the relation parameter). These values set a type of mutual relation between the two tissue classes. The model **1506** determines how to use these relations for the optimization. An example model determines that the relative volume of a tissue class should be ideally maintained along all time frames (for each specific position).

The deviation from the pure model can be calculated as follows to create a cost function: For a given position (voxel) having sets of TAC data points, calculate a mean relative volume of each tissue class (the mean is along the time frame axis), calculate a sum of squares of distances between the calculated relative volumes to the mean value, and define the tissue relation cost function as a sum of the multiple sum of squares of distances.

For the optimization, multiple cost functions are determined, one for each of the models. A cost function determines the weight in the optimization of the deviation of the actual results from the pre-defined model. An example for an optimization criterion is that the sum of all three cost functions should be minimized. The optimization process (the data modification) can be done by shifting the values of center of gravity e.g., **506** in FIG. **5**, in each time frame to the left or right of the histogram and calculating again the whole process.

An example first cost function is the sum of squares of the distances between the new set of center of gravities to the original set of center of gravities (possibly multiplied by a pre-defined constant weight). An example second cost function is the sum of the second derivatives of the two TACs

(possibly multiplied by a pre-defined constant weight). An example third cost function is the tissue relation cost function described above (possibly multiplied by a pre-defined constant weight).

Another optimization step (or an intermediate step) can be to change the TACs definition (the deviation between the representative tissue class values in block **5**) without changing the values of the center of gravity, if this contributes to the minimization of the total cost function. The direction and magnitude of changing the center of gravity **506** during the optimization is set according to the deviation of the relation parameter (for each time frame) from the model.

For example, if for a certain position and a certain time frame the relative volume of the first tissue class is larger than the calculated mean relative volume of the first TAC, and the relative volume of the second tissue class is smaller than the calculated mean relative volume of the second TAC, then during the optimization **506** should be shifted to the left of the histogram (with a pre-defined shift magnitude) to potentially reduce the volume of the first tissue class and to increase the relative volume of the second tissue class. In this way, the optimization can rapidly converge to a "best" solution.

FIG. **16** illustrates a method for separating entangled heterogeneous tissue components and generating individual TACs for the individual tissue components.

It is to be appreciated that the ordering of the acts is not limiting. As such, other orderings are contemplated herein. In addition, one or more acts may be omitted and/or one or more additional acts may be included.

At **1602**, a 4D data set of a contrast enhanced dynamic scan is obtained.

At **1604**, a histogram is generated for each spatial position (i.e., voxel or region) in the 4D data set to be evaluated for each time frame to be evaluated.

At **1606**, for each histogram, multiple distribution ranges are defined for multiple tissue components, one range for each tissue component.

At **1608**, a representative value for each range is determined.

At **1610**, a parameter relation between the multiple tissue components is determined based on the histograms and ranges.

At **1612**, a TAC is generated for each tissue component based on the representative values of each time frame and a likelihood of TAC patterns of the multiple tissue components.

At **1614**, it is determined whether a TAC optimization is to be performed.

If not, then at **1616**, a perfusion map for each class is created based on the corresponding TAC and at least one of the perfusion maps is visually presented and, optionally, relation maps are created and visually presented.

If so, then at **1618** the parameter relations are compared to a model that defines a likelihood of the parameter relation pattern between the multiple tissue components.

At **1620**, the result is checked to see whether is satisfies predetermined criteria.

If so, then act **1616** is performed.

If not, then at **1622** a set of different ranges are identified and act **1606** is repeated.

The above may be implemented by way of computer readable instructions, encoded or embedded on computer readable storage medium, which, when executed by a computer processor(s), cause the processor(s) to carry out the described acts. Additionally or alternatively, at least one of

the computer readable instructions is carried by a signal, carrier wave or other transitory medium.

The invention has been described with reference to the preferred embodiments. Modifications and alterations may occur to others upon reading and understanding the preceding detailed description. It is intended that the invention be constructed as including all such modifications and alterations insofar as they come within the scope of the appended claims or the equivalents thereof.

The invention claimed is:

1. A method, comprising:

obtaining a 4D data set in electronic format, wherein the 4D data set includes a plurality of 3D volumes of voxels of contrast enhanced perfusion imaging data for two or more time frames, and the 3D volumes include data representative of at least two different tissue components in a same region of interest in at least one of the time frames;

generating a different time activity curve point for each of the different tissue components for each voxel being evaluated for each time frame being evaluated; and

generating a signal indicative of a different parameter map for each of the different tissue components based at least on the time activity curves.

2. The method of claim **1**, further comprising:

applying a mask to a sub-portion of a 3D volume about a voxel of interest; and

generating a histogram for the voxel based on voxels within the mask,

wherein a time activity curve corresponding to the voxel is generated based on the histogram.

3. The method of claim **2**, wherein the mask applies different weights to values of different voxels based on a distance of a voxel to the voxel of interest.

4. The method of claim **2**, further comprising:

dividing the histogram into at least two different ranges, each range corresponding to a different tissue component;

calculating a representative value for each of the at least two ranges; and

determining a time activity curve point for each of the ranges, thereby determining a time activity curve for each of the different tissue components.

5. The method of claim **4**, further comprising:

determining the time activity curve based on a predetermined model that defines a likelihood of each of a plurality of different time activity curve patterns.

6. The method of claim **4**, further comprising:

determining a parameter relation between the different tissue components based on the histogram and the ranges; and

generating a second signal indicative of a different relation map for each of the different tissue components based the parameter relation.

7. The method of claim **6**, further comprising:

comparing the parameter relation to pre-determined data representing a likelihood of parameter relations between the different components;

checking a result of the comparison with pre-defined criteria; and

visually presenting at least the parameter maps in response to the results satisfying the pre-defined criteria.

8. The method of claim **7**, further comprising:

in response to the results not satisfying the pre-defined criteria:

modifying the at least two ranges, generating at least two modified ranges;

dividing the histogram into the at least two modified ranges;

calculating a subsequent representative value for each of the at least two modified ranges; and

determining a subsequent time activity curve point for each of the modified ranges, thereby determining a subsequent time activity curve for each of the different tissue components.

9. The method of claim 8, further comprising:

repeating the acts of modifying the ranges, dividing the histogram hosed on the modified ranges, calculating the subsequent representative value, and determining the subsequent time activity curve until stopping criteria is reached.

10. The method of claim 9, wherein the stopping criteria includes at least one of: a pre-defined number of iterations is reached, a difference in the results between sequential iterations is below a predetermined threshold, or a predetermined amount of time elapses.

11. A processing system, comprising:

a histogram generator configured to generate a histogram for each voxel being evaluated in a plurality of 3D volumes of voxels of contrast enhanced perfusion imaging data for two or more time frames, wherein the 3D volumes include data representative of at least two different tissue components in a same region of interest in at least one of the time frames;

a time activity curve generator configured to generate a different time activity curve point for each of the different tissue components for each voxel being evaluated for each time frame being evaluated; and

perfusion map generator configured to generate a signal indicative of a different parameter map for each of the different tissue components based at least on the time activity curves.

12. The processing system of claim 11, further comprising: a mask applier configured to apply a mask to a subportion of a 3D volume about a voxel of interest, wherein the histogram generator generates a corresponding histogram for the voxel based on voxels within the mask, and a time activity curve corresponding to the voxel is generated based on the histogram.

13. The processing system of claim 12, wherein the mask applies different weights to values of different voxels based on a distance of a voxel to the voxel of interest, wherein the weights are based on at least one of a Gaussian, binary, linear, exponential or stepped distribution.

14. The processing system of claim 12, further comprising:

a histogram evaluator configured to divide each of the histograms into at least two different ranges, each range corresponding to a different tissue component, calculates a representative value for each of the at least two ranges, and

determines a time activity curve point for each of the ranges, thereby determining a time activity curve for each of the different tissue components.

15. The processing system of claim 14, wherein the time activity curve is determined based on a predetermined model that defines a likelihood of each of a plurality of different time activity curve patterns.

16. The processing system of claim 14, further comprising:

a parameter determiner configured to determine a parameter relation between the different tissue components based on the histogram and the ranges; and

a relation map generator configured to generate a different relation map for each of the different tissue components based the parameter relation.

17. The processing system of claim 16, further comprising:

an optimizer, including:

an analyzer configured to compare the parameter relation to pre-determined data representing a likelihood of parameter relations between the different; components; and

a criteria checker configured to check a result of the comparison with pre-defined criteria, and

a rendering engine configured to visually present at least the parameter maps in response to the results satisfying the pre-defined criteria.

18. The processing system of claim 17, wherein, in response to the results not satisfying the pre-defined criteria, the histogram evaluator divides the histogram into the at least two modified ranges, calculates a subsequent representative value for each of the at least two modified ranges, and determines a subsequent time activity curve point for each of the modified ranges, thereby determining a subsequent time activity curve for each of the different tissue components.

19. The processing system of claim 18, wherein the histogram evaluator repeats the acts of modifying the ranges, dividing the histogram based on the modified ranges, calculating the subsequent representative value, and determining the subsequent time activity curve until stopping criteria is reached.

20. A non-transitory computer readable storage medium encoded with one or more computer executable instructions, which, when executed by a processor of a computing system, causes the processor to:

obtain a 4D data set in electronic format, wherein the 4D data set includes a plurality of 3D volumes of voxels of contrast enhanced perfusion imaging data for two or more time frames, and the 3D volumes include data representative of at least two different tissue components in a same region of interest in at least one of the time frames;

generate a different time activity curve point for each of the different tissue components for each voxel being evaluated for each time frame being evaluated; and

generate a signal indicative of a different parameter map for each of the different tissue components based at least on the time activity curves.

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